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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/764,359

Applicant(s)

REID ET AL.

Examiner

Quang Nguyen, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 January 2003 and 05 June 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 10,22 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9,11-21,23-36 and 38-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's election of the following species: a) liver as a donor tissue; b) adult as a donor; and c) hepatic progenitor cell lineage in Paper No. 14 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the species restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-40 are pending in the present application.

Claims 10, 22 and 37 are withdrawn from further consideration because they are drawn to non-elected species.

Accordingly, claims 1-9, 11-21, 23-36 and 38-40 are examined on the merits herein.

### ***Specification***

The specification is objected because it is inappropriate for the entire sequence listing to be inserted in on page 44, lines 20-28 (See Amendment B). Examiner suggests that the sequence listing should be filed separately, and on page 44, lines 20-28, appropriate SEQ ID NOs. should be assigned to the listed sequences. For example, insert the phrase -- (SEQ ID NO. 1) -- between "3'" and "," on line 20 of page 44, and so on. Appropriate correction is required.

***Information Disclosure Statements***

The references listed in the IDS filed on 2/8/02 in Paper No. 7 are not present with the application. Therefore, examiner has not considered all the references listed. Should Applicants wish examiner to consider all the listed references, substitute copies of the references that have not been considered are requested.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-7, 11, 13-15, 23-36 and 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and its dependent claims, it is unclear what is encompassed by the phrase "non-fetal donor tissue that would be considered unsuitable for an organ transplantation" is unclear. Which conditions or criteria are used for considering a non-fetal donor tissue to be unsuitable or suitable for organ transplantation? These criteria are not explicitly defined in the specification and are inherently subjective. The metes and bounds of the claims are not clearly determined.

The terms "substantially single cell suspension", "substantially enriched" in claims 12, 23 and its dependent claims, respectively, are relative terms which render the claims indefinite. The terms "substantially single cell suspension" and "substantially enriched" are not defined by the claim, the specification does not provide a standard for

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ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Therefore, the metes and bounds of the claims are not clearly determined. Similarly, the term "substantially enriched" is also recited in claim 39 and its dependent claim 40.

Claim 13 is dependent on itself. Therefore, claim 13 and its dependent claims 14-15 are indefinite because it is not clear what exactly Applicants claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 11-12, 16-17, 19-20 and 39-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Reid et al. (WO 95/13697; 1995; IDS).

With respect to the elected species, Reid et al. disclose methods for isolating hepatoblasts comprising liver stem cells (pluripotent precursors) and committed precursors for either hepatocytes and bile duct cells using panning technologies and multiparametric FAC sorting from a single cell suspension of liver cells (see Summary of

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Invention). Reid et al. state "The methods of the invention have been developed using embryonic and neonatal livers from rats, however, the method of the invention offers a systemic approach to isolating hepatoblasts from any age from any species" (page 4, lines 6-10). This statement includes the isolation of hepatoblasts from adult liver (see page 43). Reid et al. also note that hepatoblasts which are found in a high proportion of liver cells in early embryonic livers and in small number located periportally in adult livers (page 3, line 35 continues to line 1 of page 4). In the disclosed method (page 14, lines 9-15 for example), livers were dissected from donors (the donors should no longer have any heart-beat as a consequence of the removal or from the dissection of the livers), and placed into fresh ice-cold HBSS (should be about 4°C). Additionally, since the livers from the donors are harvested immediately, the liver tissues were obtained within the recited time windows (within about 6 hrs, about 3 hrs, or about 1 h). Reid et al. also teach that the tendency of the isolated cells to aggregate is prevented by maintaining the cells at 4°C and by removing calcium with EGTA (page 39, lines 24-33). The isolated hepatoblast cell populations prepared by the methods taught by Reid et al. are indistinguishable from the composition comprising a population of cells enriched in diploid cells, including progenitors that express alpha-fetoprotein of the presently claimed invention.

Accordingly, the teachings of Reid et al. meet all the limitations of the instant claims, and therefore the claims are anticipated by WO 95/13697.

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Claims 1-2, 8-9, 11-12, 16-21, 23-26 and 38-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Faris (U.S. 6,129,911 with the effective filing date of 7/10/1998).

With respect to the elected species, Faris teach methods for isolating liver cell clusters comprising a liver stem cell and a hepatocyte, and a population of isolated liver stem cells, wherein the stem cells can differentiate into hepatocytes or bile ductal cells (see Summary of the Invention). The isolated liver cell clusters and isolated stem cells are obtained from adult liver tissue from various species such as a mouse, a pig or a human; and that the liver tissue is obtained from deceased donors or cadavers (these donors do not have heart-beats, see col. 5, lines 3-25). Faris teaches that the liver cell clusters are dissociated by enzymatic disruption to destroy the desmosomal junctions, and that the isolated liver stem cells can be further purified using magnetic beads coated with antibodies specific for selective cell markers or FACS sorting (col. 6, lines 54-67).

The methods and compositions taught by Faris meet all the limitation of the instant claims, and therefore U.S. Patent No. 6,129,911 anticipates the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 23-28, 33-36 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reid et al. (WO 95/13697; 1995; IDS) in view of Faris (U.S. 6,129,911).

Reid et al. disclose methods for isolating hepatoblasts comprising liver stem cells (pluripotent precursors) and committed precursors for either hepatocytes and bile duct cells using panning technologies and multiparametric FAC sorting from a single cell suspension of liver cells (see Summary of Invention, and examples). Reid et al. state "The methods of the invention have been developed using embryonic and neonatal livers from rats, however, the method of the invention offers a systemic approach to isolating hepatoblasts from any age from any species" (page 4, lines 6-10). This statement includes the isolation of hepatoblasts from adult liver (see page 43). Reid et al. also note that hepatoblasts which are found in a high proportion of liver cells in early embryonic livers and in small number located periportal in adult livers (page 3, line 35 continues to line 1 of page 4).



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Reid et al. do not teach specifically that the donor has a non-beating heart at a time when the liver tissue is harvested, or that the liver tissue is harvested within about six, three, two or one hour after the heartbeat has ceased.

However, at the effective filing date of the present application Faris already teach that human liver tissue obtained from cadavers (do not have any heartbeats) was used as a source of tissue for the preparation of liver stem cells and liver cluster cells (col. 5, lines 21-23). Faris teaches specifically that it is preferred that the cells are obtained from adult liver tissue rather than the fetal tissue (col. 2, lines 7-10).

Accordingly, at the effective filing date of the present application, it would have been obvious for an ordinary skilled artisan in the art to modify the method taught by Reid et al. by using adult liver tissues obtained from cadavers for the preparation of hepatoblasts comprising liver stem cells (pluripotent precursors) and committed precursors for either hepatocytes and bile duct because Faris already teach that human liver tissue obtained from cadavers was used for the isolation of liver stem cells and liver cluster cells.

One of ordinary skilled artisan would have been motivated to carry out the above modification because cadavers provide a large source of liver tissue for the preparation or isolation of liver hepatoblasts or stem cells. Additionally, one of ordinary skilled artisan would have been motivated to obtain liver tissues from fresh cadavers (e.g., within the recited time periods after the heartbeat ceased) to minimize damages to the resident liver hepatoblast or stem cell populations.

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Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### **Conclusions**

***No claims are allowed.***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

  
PATENT EXAMINER